L2: Entry 4 of 4

File: USPT

Jun 2, 1998

DOCUMENT-IDENTIFIER: US 5759551 A
TITLE: Immunogenic LHRH peptide constructs and synthetic universal immune stimulators for vaccines

Detailed Description Text (4):
2. Addition of Spacer Residues Between Immunogenic Elements. Immunogenicity can be improved through the addition of spacer residues (e.g. Gly-Gly) between the promiscuous T.sub.h epitope and LHRH. In addition to physically separating the T.sub.h epitope from the B cell epitope (i.e., LHRH), the glycine residues can disrupt any artificial secondary structures created by the joining of the T.sub.h epitope with LHRH--and thereby eliminate interference between the T and/or B cell responses. The conformational separation between the helper epitope and the antibody eliciting domain thus permits more efficient interactions between the presented immunogen and the appropriate T.sub.h and B cells.

Detailed Description Text (245):
T cell activation can also be brought about by LHRH that is covalently linked to a specific fragment from the invasin protein of the pathogenic bacteria Yersinia spp. Peptide 32, in which a domain of the invasin protein is linked to the HBs T.sub.h epitope: LHRH construct (i.e. Inv.sub.718-732 +peptide 18) has been synthesized. Peptide 32 is organized in five linear domains, from the amino- to the carboxyl-terminus, as follows: the invasin T cell stimulator (Inv), a glycine spacer (GG), the hepatitis B surface antigen helper T cell epitope (HBsAg T.sub.h 1), a glycine spacer (GG), and LHRH. Peptide 32 is thus represented as: Inv: GG: HBsAg T.sub.h 1: GG: LHRH. The following provides a specific example of the significant efficacy imparted to the LHRH immunogen by the addition of the invasin domain. The experimental design is the same as in Example 5 except as indicated otherwise.
Experimental Design:

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End of Result Set

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L2: Entry 1 of 4 File: USPT Nov 27, 2001

DOCUMENT-IDENTIFIER: US 6322789 B1
TITLE: HLA-restricted hepatitis B virus CTL epitopes

Detailed Description Text (27):
In an exemplary embodiment described below, a T helper peptide from substantially within HBc.sub.128-140 (Thr-Pro-Pro-Ala-Tyr-Arg-Pro-Pro-Asn-Ala-Pro-Ile-Leu) [Seq. ID No. 19]), when linked with the CTL peptide (HBc18-27), was shown to induce specific CTL priming of animals in all animals studied, and at levels which were greater than when the CTL peptide and T helper peptide were administered unlinked. When the T helper and CTL HBV peptides were linked by a Ala-Ala-Ala spacer, specific CTL activity greater than induction of specific CTL activity with the linked peptides without spacer. These results suggest enhanced CTL response against cells which display HBV antigens when the peptide containing a CTL epitope is linked via spacer to a peptide containing a HBV T helper epitope is used as the immunogen.

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L3: Entry 18 of 25

File: USPT

Mar 3, 1998

DOCUMENT-IDENTIFIER: US 5723129 A
TITLE: GnRH-leukotoxin chimeras

Detailed Description Text (35):
Furthermore, the particular GnRH portion depicted in FIG. 1B SEQ ID NOs:3-4 contains spacer sequences between the GnRH moieties. The present invention particularly contemplates the strategic use of various spacer sequences between selected GnRH polypeptides in order to confer increased immunogenicity on the subject constructs. Accordingly, under the invention, a selected spacer sequence may encode a wide variety of moieties of one or more amino acids in length. Selected spacer groups may preferably provide enzyme cleavage sites so that the expressed chimera can be processed by proteolytic enzymes in vivo (by APC's or the like) to yield a number of peptides-each of which contain at least one T-cell epitope derived from the carrier portion (leukotoxin portion)--and which are preferably fused to a substantially complete GnRH polypeptide sequence. Further, spacer groups may be constructed so that the junction region between selected GnRH moieties comprises a clearly foreign sequence to the immunized subject, thereby conferring enhanced immunogenicity upon the associated GnRH peptides. Additionally, spacer sequences may be constructed so as to provide T-cell antigenicity, such as sequences which encode amphipathic and/or .alpha.-helical peptide sequences which are generally regarded in the art as providing immunogenic helper T-cell epitopes. In this regard, the choice of particular T-cell epitopes to be provided by such spacer sequences may vary depending on the particular vertebrate species to be vaccinated. Although, particular GnRH portions are exemplified which include spacer sequences, it is also contemplated herein to provide a GnRH multimer comprising directly adjacent GnRH sequences (without intervening spacer sequences).

CLAIMS:

6. The chimeric protein of claim 5 wherein X comprises an amino acid spacer group including at least one helper T-cell epitope.

L2 ANSWER 28 OF 28 MEDLINE
AN 90038212 MEDLINE
DN 90038212 PubMed ID: 2681356
TI An antiserum to the N-terminal subsequence of the Alzheimer amyloid beta protein does not react with neurofibrillary tangles.
AU Behrouz N; Defossez A; Delacourte A; Hublau P; Mazzuca M
CS National Institute of Health and Medical Research (INSERM 156), University of Lille II, France.
SO JOURNAL OF GERONTOLOGY, (1989 Nov) 44 (6) B156-9.
Journal code: 0374762. ISSN: 0022-1422.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198912
ED Entered STN: 19900328
Last Updated on STN: 19980206
Entered Medline: 19891221
AB Polyclonal antibodies were raised against a synthetic peptide corresponding to a subsequence for the first 10 residues of the **beta amyloid** protein A4 (**1-10** beta PA4). In an immunoperoxidase study of Alzheimer brain tissue, these antibodies immunostained senile plaque cores, amyloid vessel walls, and amyloid fibrils surrounding senile plaques and angiopathic vessels. Neurofibrillary tangles stained with thioflavin S or immunostained with anti-Tau immune serum were never immunodetected with the anti **1-10** beta PA4. We confirm that the neurofibrillary tangles do not contain epitopes corresponding to the first 10 residues of the beta PA4.

L2 ANSWER 15 OF 58 MEDLINE
AN 2000181291 MEDLINE
DN 20181291 PubMed ID: 10718363
TI Relative sensitivity of undifferentiated and cyclic adenosine 3',5'-monophosphate-induced differentiated neuroblastoma cells to cyclosporin A: potential role of **beta-amyloid** and ubiquitin in neurotoxicity.
AU Kumar A; Hovland A R; La Rosa F G; Cole W C; Prasad J E; Prasad K N
CS Center for Vitamins and Cancer Research and Department of Radiology, College of Medicine, University of Colorado Health Sciences Center, Denver 80262, USA.
NC RO1 NS29982 (NINDS)
RO1 NS35348 (NINDS)
SO IN VITRO CELLULAR AND DEVELOPMENTAL BIOLOGY. ANIMAL, **(2000 Feb)** 36 (2) 81-7.
Journal code: 9418515. ISSN: 1071-2690.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200005
ED Entered STN: 20000525
Last Updated on STN: 20000525
Entered Medline: 20000518
AB Cyclosporin A is routinely used in transplant therapy following allogeneic or xenogeneic tissue transplantation to prevent rejection. This immunosuppressive drug is also neurotoxic; however, its mechanisms of action for neurotoxicity are poorly understood. Undifferentiated and cyclic adenosine 3',5'-monophosphate (cAMP)-induced differentiated neuroblastoma (NB) cells were used as an experimental model to study the toxicity of cyclosporin A. Results showed that cyclosporin A promoted the outgrowth of neurites and inhibited the growth of undifferentiated NB cells. When cyclosporin A was added simultaneously with RO20-1724, an inhibitor of cyclic nucleotide phosphodiesterase, or with prostaglandin E1, a stimulator of adenylate cyclase, it markedly enhanced the growth inhibitory and differentiation effects of these cAMP-stimulating agents. In addition, cyclosporin A added to cAMP-induced differentiated NB cells caused dose-dependent degeneration of these cells as evidenced by the vacuolization of cytoplasm and the fragmentation of nuclear and cytoplasmic materials; however, neurites remained intact. Cyclosporin A alone did not alter the intensity of cell immunostaining for ubiquitin or **beta-amyloid** peptide (amino acids **1-14**) (Abeta1-14); however, it enhanced the intensity of staining for both ubiquitin and Abeta in cells that were treated with cAMP-stimulating agents. The intensity of staining of amyloid precursor protein (amino acids 44-63) (APP44-66) did not change in any treated group, suggesting that the increase in Abeta staining is due to increased processing of APP to Abeta. We propose that one of the mechanisms of cyclosporin A-induced neurotoxicity involves increased levels of Abeta and ubiquitin.